RESEARCH ARTICLE / *Araştırma Makalesi*

Relation of High Sensitive Troponin-I and C-reactive Protein to Mortality in Patients with COVID-19

Yüksek Sensitive Troponin-I ve C-Reaktif Protein ile COVID-19 Hastalarındaki Mortalite Arasındaki İlişki

Mahmut Akpek

Department of Cardiology, Parkhayat Kutahya Hospital, Kutahya, Turkey

Yazışma Adresi / *Correspondence:*
Mahmut Akpek

Parkhayat Kutahya Hospital, Department of Cardiology, Kutahya, TURKEY
T: **+90 274 202 02 02** E-mail **: mahmutakpek@yahoo.com**

Geliş Tarihi / Received : **10.06.2021** Kabul Tarihi / Accepte: **16.02.2022**

Orcid :
Mahmut Akpek https://orcid.org/0000-0002-2867-4993

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2022, 12(1):85-91) DOI: 10.31832/smj.950632**

Abstract

Objective	The aim of the present study is to investigate whether the high sensitive troponin-I (HsTrop-I) and C-reactive protein (CRP) level that measured on admission is an independent predictor of mortality in patients with coronavirus disease 2019 (COVID-19).
Materials and Methods	In this retrospective,cross-sectional and descriptive study, a total of 175 consecutive patients with confirmed COVID-19 cases were screened from November 01, 2020 to January 31, 2021. Finally, 137 eligible patients were enrolled in to the study. Data of patients were recorded from the electronic medical records and National health data registry.
Results	Mean age of study population was 49.7 ± 14.8 year and 88 (64.2%) patients were female. A HsTrop-I level ≥21.6 pg/ml measured on admission had a 86% sensitivity and 88% specificity in predicting mortality. The CRP level ≥80.8 mg/l on admission predicted mortality with 86% sensitivity and 95% specificity in patients with COVID-19. In the multivariate analyzes, HsTrop-I (odds ratio (OR) 1.124, 95% confidence interval (CI) 1.025–1.232; p=0.013) and CRP (OR 1.060, 95% CI 1.021–1.100; p=0.002) on admission were independent predictors of mortality in patients with COVID-19.
Conclusion	HsTrop-I and CRP levels on admission which are easily measurable laboratory data were independent predictors of mortality in patients with COVID-19. Therefore, HsTrop-I and CRP levels could help to physicians for earlier triage of the patients that potentially worsening and may lead to provide the effective use of health resources.
Keywords	Coronavirus; High sensitive troponin-I; Mortality

Öz

Amaç	*Bu çalışmanın amacı, başvuru sırasında ölçülen yüksek sensitif troponin-I (YsTrop-I) ve C-reaktif proteinin (CRP) düzeylerinin Koronavirüs 2019 hastalığına (KOVID-19) bağlı ölüm ile bağımsız ilişkili olup olmadığını araştırmaktır.*
Gereç ve Yöntemle	*Retrospektif ve kesitsel tipte tanımlayıcı olarak tasarlanan bu çalışma için, 01 Kasım 2020 ile 31 Ocak 2021 tarihleri arasında KOVID-19 tanısı konulmuş toplam 175 hasta tarandı. Sonuç olarak, 137 uygun hasta çalışmaya dâhil edildi. Hasta verileri hastanenin elektronik kayıtlarından ve ulusal sağlık bilgi bankasından kaydedildi.*
Bulgular	*Çalışma populasyonunun ortala yaşı 49.7 ± 14.8 yıl ve 88 (%64.2) hasta kadındı. KOVID-19 hastalarında başvuru anında ölçülen YsTrop-I değerinin ≥21.6 pg/ml olması mortaliteyi %86 duyarlılık ve %88 özgüllük ile öngörme gücüne sahipti. Başvuru anında ölçülen CRP değerinin ≥80.8 mg/l olması mortaliteyi %86 duyarlılık ve %95 özgüllük ile öngörme gücüne sahipti. Çoklu analizde; başvuru anında ölçülen YsTrop-I (Risk oranı (RO) 1.124,% 95 Güven aralığı (GA) 1.025–1.232; p=0.013) ve CRP (RO 1.060, %95 GA 1.021–1.100; p=0.002) KOVID-19 hastalarında mortalitenin bağımsız öngördürücüleriydi.*
Sonuç	*Başvuru anında kolaylıkla ölçülebilen YsTrop-I ve CRP değerleri KOVID-19 hastalığına bağlı mortalitenin bağımsız öngördürücüsüdür. Dolayısıyla, YsTrop-I ve CRP, kötüleşebilme potansiyeline sahip hastaların erken tespit edilmesinde ve sağlık kaynaklarının daha verimli kullanılmasında doktorlara yardımcı olabilir.*
Anahtar Kelimeler	*Koronavirüs; Yüksek sensitif troponin-I; Mortalite*

INTRODUCTION

From December 2019, the coronavirus disease 2019 (Covid-19) outbreak has become a major challenge for public health. COVID-19 is caused by a novel coronavirus known as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The number of new cases continues to increase and more than two million people died due to COVID 19 pandemic to date.[1-3] Data from studies and clinical experiences around the world have focused on efforts to determine the better treatment protocol and reduce the mortality due to COVID-19. Several studies showed that numareous biomarkers, such as C-reactive protein, D-dimer, leukocyte, procalcitonin, interleukin 10 and interleukin 6 increase with the initiation and the progression of the COVID-19.[4-6] In a recent study, Zhang et al. showed that D-dimer level on admission greater than 2.0μg/mL is a predictor of the in-hospital mortality of COVID-19.[4] Imam et al. suggested that advanced age and increasing number of co-morbidities including hypertension and chronic kidney disease are independent predictors of in-hospital mortality for COVID-19 patients.[7] On the other hand, during the outbreak, high volume of new COVID-19 cases presenting to hospitals above their capacities requires effective risk stratification. New independent predictors of disease severity and the mortality of COVID-19 should be investigated in order to make earlier triage and to help clinicians for effective treatment management. For this purpose, the present study aimed to investigate the prognostic role of high sensitive Troponin-I (HsTrop-I) and CRP levels measured on admission in COVID-19 related mortality.

MATERIALS and METHODS

The present study is a single-center, cross-sectional, descriptive and has a retrospective design. A total of 175 consecutive patients with confirmed COVID-19 from November 01, 2020 to January 31, 2021 were screened. The patients under the age of 18, with systemic inflammatory disease history, previous kidney and liver failure history, with coronary artery disease history and with missing data were excluded. Finally, 137 eligible patients were enrolled in to the study (Figure 1).

The confirmed diagnosis of COVID-19 was defined as the detection the presence of ribonucleic acid on the nasopharyngeal and oropharyngeal swab of severe acute respiratory syndrome coronavirus-2 by reverse transcriptase polymerase chain reaction in the Public Health Microbiology Laboratory of the Ministry of Health according to World Health Organization guidance.[8] Nasopharyngeal and oropharyngeal swab samples were collected at the time of admission to the COVID-19 outpatient unit.

The demographics, comorbidities, initial routine laboratory results, treatment protocol and outcome data of patients were recorded from the electronic medical records of Parkhayat Kutahya hospital and National health data registry (e-Nabız®). In all patients, antecubital venous blood samples for routine laboratory analysis were drawn upon admission. Complete blood count, CRP, HsTrop-I, creatinine, D-dimer, ferritin, lactate dehydrogenase (LDH), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured in central laboratories of Parkhayat Kutahya hospital.

Complete blood count was measured with ELite 580 advanced hematology analyzer (Erba, Czech Republic). C-reactive protein, lactate dehydrogenase (LDH), alanine aminotransferase (ALT) and aspartate aminotransferase (AST), creatinine, were measured by Beckman Coulter AU 640 (Japan) analyzer. Ferritin and HsTrop-I were measured by Beckman Coulter DXI 800 (Japan) analyzer. D-dimer was determined with the Getein 1600 immunofluorescence quantitative analyzes (China).

Decision and the management of the treatment protocol was left to the discretion of pandemic team consisting of infection disease, radiology, chest disease, anesthesiology, cardiology and internal medicine specialized medical doctors and pharmacist in the light of updated guideline by the Turkish Ministry of Health. Steroid therapy was defi-

ned as up to 100 mg methylprednisolone or 8 mg dexamethasone administration. High dose of steroid therapy was defined as more than 250 mg methylprednisolone administration for up to 5 days. The present study was approved by the Kutahya Health Science University ethics committee (Date: 06.04.2021, Number: E-41997688-050.99-8877). Continuous variables were tested for normal distribution by the Kolmogorov-Smirnov test. The variables are expressed as means ± standard deviation or median (interquartile range). The Receiver Operating Characteristics (ROC) curve was used to demonstrate the sensitivity and specificity of CRP and HsTrop-I their respective, optimal cut-off value for predicting mortality in patients with COVID-19. The effects of different variables on mortality due to COVID-19 were calculated in univariate logistic regression analysis for each. The variables for which the unadjusted P value was <0.10 were identified as potential risk markers. Therefore, age, CRP, HsTrop-I, ferritin, LDH and white blood cell count (WBC) were included in the full model. We reduced the model by using backward elimination multivariate logistic regression analyses with backward selection. All statistical analyses were performed using the SPSS statistical package for Windows version 15.0 (SPSS Inc., Chicago, IL, USA). P value <0.05 was considered as significant and confidence interval (CI) was 95%.

RESULTS

There were 137 confirmed COVID-19 patients (mean age 49.7 ± 14.8) in the present study. The 88 patients (64.2%) were female. Baseline characteristics are shown in Table 1. In the laboratory status on admission, the hemoglobin level was 13.5 ± 1.8 gr/dL, white blood cell count was 5.45 10^3/uL (4.05 - 6.08) and lymphocyte count was 1.51 ± 0.56 10^3/uL. Serum level of CRP was 5.30 (2.06 – 18.35) mg/L, HsTrop-I was 17.90 (17.10 – 19.25) pg/ml and D-dimer was 170 ng/ml (104.7 – 463.0) on admission. Serum levels of other biochemical parameters were shown in Table 1. Greater proportion of patients was on favipiravir (83.2%) chloroquine/hydroxychloroquine treatment (70.8%), while only 44 patients were on azithromycin treatment (32.1%). Steroid therapy required in only 17 patients (12.4%) and 62 patients (45.3%) were on low molecular weight heparin treatment. High dose of steroid and tocalizumab were administered for only 3 (2.2%) and 6 (4.4%) patients in intensive care unit, respectively. With respect to previous comorbidities, 27 of patients had hypertension (19.7%), 18 of patients had diabetes mellitus (13.1%) and 9 of patients had chronic obstructive pulmonary disease (6.6%).

Table 1. Baseline characteristics

	n = 137
Age, year	49.7 ± 14.8
Female, n (%)	88 (64.2%)
Outpatient follow-up/Hospitalization, n (%)	109 (79.6%) / 28 (20.4%)
Hospital stay, day	8.5 ± 3.7
Mortality, n (%)	7 (5.1%)
Laboratory findings	
Hemoglobin, gr/dL	13.5 ± 1.8
White blood cell, 10^3/uL	5.45 (4.05 – 6.08)
Lymphocyte, 10^3/uL	1.51 ± 0.56
C-reactive protein, mg/l	5.30 (2.06 – 18.35)
High sensitive troponin-I, pg/ml	17.90 (17.10 – 19.25)
D-Dimer, ng/ml	170.0 (104.7 – 463.0)
Ferritin, ng/ml	50.0 (25.4 – 120.9)
Lactate dehydrogenase, U/L	159.0 (120.0 – 204.0)
Creatinine, mg/dL	0.93 (0.80 – 1.10)
Alanine aminotransferase, U/L	21.0 (15.0 – 39.0)
Aspartate aminotransferase, U/L	26.0 (21.0 – 36.0)
Medications	
Favipiravir, n (%)	114 (83.2%)
Chloroquine/hydroxychloroquine, n (%)	97 (70.8%)
Azithromycin, n (%)	44 (32.1%)
Anti-coagulant use, n (%)	62 (45.3%)
Steroid, n (%)	17 (12.4%)
High dose of steroid, n (%)	3 (2.2%)
Tocilizumab, n (%)	6 (4.4%)
Previous medical history	
Hypertension, n (%)	27 (19.7%)
Diabetes Mellitus, n (%)	18 (13.1%)
Chronic obstructive pulmonary disease, n (%)	9 (6.6%)

The ROC curves of HsTrop-I and CRP for predicting mortality are shown in Figure 2. A HsTrop-I level ≥ 21.6 pg/ml measured on admission had a 86% sensitivity and 88%

specificity in predicting mortality (p<0.001). The CRP level ≥80.8 mg/l on admission predicted mortality with 86% sensitivity and 95% specificity in patients with COVID-19 (p<0.001).

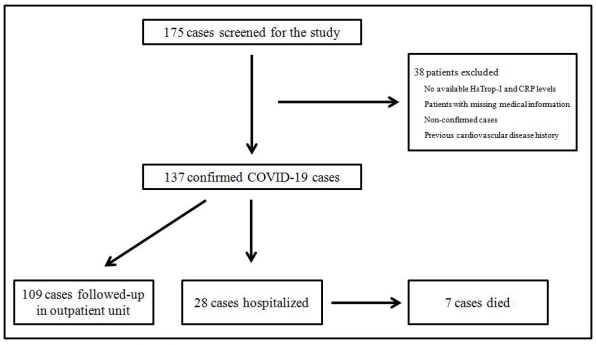

Figure 1. Study diagram

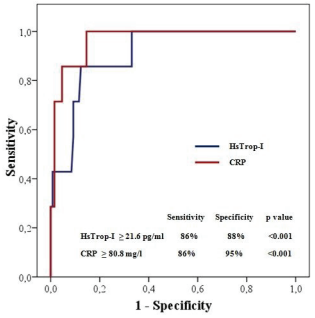

Figure 2. The receiver-operating characteristic curve of high sensitive troponin for predicting mortality in patients with COVID-19.

In the baseline characteristics and laboratory findings on admission of the patients; some of variables that can be effective on mortality were seen in some of patients. So, the effects of multiple variables on the mortality analyzed with univariate and multivariate logistic regression analyses (Table 2 and Table 3, respectively). The variables for which the unadjusted p value was <0.10 in univariate analysis were identified as potential risk markers for mortality and included in the full model for the evaluation of independency. Age, CRP, HsTrop-I, ferritin, LDH, WBC count and previous chronic obstructive pulmonary disease history were analyzed with multivariate logistic regression model. After multivariable adjustment, HsTrop-I (odds ratio (OR) 1.124, 95% confidence interval (CI) 1.025–1.232; p=0.013) and CRP (OR 1.060, 95% CI 1.021–1.100; p=0.002) on admission were still independent predictors of mortality in patients with COVID-19 (Table 3).

Table 2. Univariate logistic regression analysis on the risk factors associated with mortality in COVID-19 patients

	Odds ratio	95% Confidence interval	p value
Age	1.140	1.055 - 1.233	0.001
Female	2.519	0.240 - 11.747	0.240
C-reactive protein	1.050	1.025 - 1.075	<0.001
D-Dimer	1.000	1.000 - 1.001	0.183
High sensitive troponin-I	1.102	1.047 - 1.159	<0.001
Ferritin	1.002	1.000 - 1.004	0.030
Lactate dehydrogenase	1.010	1.002 - 1.012	0.010
Hemoglobin	0.770	0.496 - 1.194	0.242
White blood cell	1.521	1.168 - 1.980	0.002
Lymphocyte	0.705	0.167 - 2.975	0.634
Hypertension	1.680	0.308 - 9.167	0.549
Diabetes Mellitus	0.001	0.001 - 1.000	0.998
Chronic obstructive pulmonary disease	7.029	1.153 – 42.864	0.035

Table 3. Multivariate logistic regression analysis on the risk factors associated with mortality in COVID-19 patients

	Odds ratio	95% Confidence interval	p value
Age	1.062	0.939 - 1.202	0.336
C-reactive protein	1.060	1.021 - 1.100	0.002
High sensitive troponin-I	1.124	1.025 - 1.232	0.013
Ferritin	1.000	0.991 - 1.008	0.925
Lactate dehydrogenase	0.991	0.980 - 1.002	0.097
White blood cell	1.054	0.722 - 1.539	0.785
Chronic obstructive pulmonary disease	1.560	0.022 – 108.918	0.837

DISCUSSION

As of March 2021, there have been more that 110,000,000 confirmed cases of COVID-19 globally, including 2,527,891 deaths, reported by World Health Organization (WHO).[1] Up to present, it has not been defined disease-specific treatment, yet. However, some vaccines have been approved for use authorization. Confirmed mutant

viruses showed that the storm has not started to subside yet. With the COVID-19 outbreak, very high volume of patients had to admit to hospital in a short time. It is overwhelms for the health professionals and hospital capabilities. In addition, critical care support effectiveness for severe disease may decrease. Since the pandemic started, published data focused on to determine the optimal treatment protocol to reduce the mortality rate in COVID-19. Recent studies also focused on the determination of independent predictors of mortality in patients with COVID-19 for the risk stratification. For this purpose, the present study was designed to evaluate the independent relation of HsTrop-I and CRP levels on admission with mortality in COVID-19 patients.

Inflammatory process is a well established issue in COVID-19. Various studies that published during the outbreak showed the independent relation of CRP with the mortality in patients with COVID-19.[5,6,9,10] The present study confirmed the previous studies and showed that CRP level on admission is independently associated with mortality in COVID-19. With the growing understanding the relation of SARS-CoV-2 and cardiovascular system, studies focused on the myocardial involvement in patients with COVID-19.[11-13] Recently, Shah et al. conducted a study to test the prognostic value of troponin-I to predict the worse outcomes in hospitalized patients with COVID-19.[11] However, they did not test the relation of numerical value of troponin-I level with the outcomes. They tested the relation of presence of cardiac injury as a categorical variable according to the highest values of cTnI for the analysis during hospitalization. The patients with the previous cardiovascular disease history were also enrolled in to the study. Therefore, it seems that the study population consisted from high risk COVID-19 patients. In the present study, patients with previous cardiovascular disease history were excluded. Study population was consisted from unselected consecutive patients. Therefore the results of our study reflect the real world scenario. In another study that conducted by Shi et al., cardiac injury was seen in the 19.7% of patients with COVID-19.[1]2 They enrolled 416 patients in to the study and they divided the study population into two groups whether the presence of cardiac injury (defined as the higher levels of HsTrop-I than the 99th percentile upper reference limit) or not. They demonstrated that the presence of cardiac injury is independently associated with the mortality in patients with COVID-19. In the present study, patients were not categorized according to references limit of HsTrop-I levels. HsTrop-I levels itself on admission, as a continues variable, independently associated with mortality in patients with COVID-19.

Cardiac involvement is a certain issue in COVID-19, but the exact mechanism of action is still controversial.[12,14,15] Studies suggest that several mechanisms are responsible for the cardiac involvement in COVID-19. One possible mechanism is the direct effect of the SARS-CoV-2. The angiotensin converting enzyme 2 (ACE2) receptors that are also the entry receptor of SARS-CoV-2 are highly expressed in the heart.[14,15] Therefore, it is rationale to suggest that the cardiac injury and the increase of troponin-I levels in COVID-19 may result from the direct effects of the virus itself via causing infectious myocarditis.[15,18] In a case report, doctor Alhogbani demonstrated that Middle east respiratory syndrome coronavirus causes acute myocarditis.[19] Second, the hypercoagulation state due to pro-inflammatory response and hypoxia may lead the occlusive micro-thrombus formations in coronary arteries in patients with COVID-19. Third, as seen in type 2 myocardial infarction, increased oxygen demand or decreased oxygen supply may lead to myocardial injury in COVID-19 patients.[20] As stated before, the exact mechanism of myocardial injury is not fully elucidated yet. It can be speculate that the direct effect of SARS-CoV-2 infection in myocardium can be responsible for cardiac involvement in the early phase of COVID-19, while microthrombus formation that the results of prothrombotic system activation and type 2 myocardial infarction can be responsible for cardiac involvement in the late phase of COVID-19. Therefore, it is clearly known that further evidence need to clarify the

exact mechanism of the myocardial injury in patients with COVID-19.

The main limitation of the present study is the retrospective fashion. Because of high infectivity of SARS-CoV-2 and logistical limitations, procedures like echocardiography and electrocardiography were avoided when they did not contribute to treatment protocol. The detailed immunologic evaluation with the cytokine levels could provide a better understand of the mechanism of cardiac involvement in COVID-19. The other limitation of the present study was being a single-center experience and represents a small number of patients. However, our study population contains homogeneous unselected COVID-19 patients, therefore mirroring the real world scenario.

In conclusion; it was demonstrated that HsTrop-I and CRP levels on admission are independent predictors of mortality in patients with COVID-19. Accordingly, HsTrop-I and CRP levels which are easily measurable laboratory data can be used as a prognostic factor. The clinical implication of the present study is that HsTrop-I and CRP levels on admission could help to physicians for the risk stratification to determine and manage the treatment protocol. The risk stratification could also lead to earlier triage of the potentially worsen patients and the effective use of health resources. Further prospective studies should be planned in order to clarify the exact mechanism of cardiac injury and to confirm the relation of HsTrop-I and mortality in patients with COVID-19.

Financial Support: This research received no specific grant from any funding agency, commercial, or not for profit sectors.

Conflicts of Interest

None.

The present study was approved by the Kutahya Health Science University ethics committee (Date: 06.04.2021, Number: E-41997688-050.99-8877).

References

1. *WHO. Coronavirus disease 2019 (COVID-19) Situation Dashboard [Internet]. Available at: https://covid19.who.int/ (Last accessed March 03, 2021).*
2. *Dervisoglu P, Elmas B, Ozdemir O, Orhan MF. Evaluation of Electrocardiographic Changes and Laboratory Parameters in Pediatric COVID-19. Sakarya Med J 2020;4:541-8*
3. *Cekic D, Senocak D, Issever K, Cekic S, Yaylaci S, Karabay O, et al. Is Hba1c and Lipid Profile A Predictor Of Determining Intensive Care Need and Mortality In Diabetic Covid-19 Patients? Sakarya Med J 2021;2:293-8.*
4. *Zhang L, Yan X, Fan Q, Liu H, Liu X, Liu Z, et al. D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. J Thromb Haemost 2020;18:1324-9.*
5. *Wan S, Yi Q, Fan S, Lv J, Zhang X, Guo L, et al. Relationships among lymphocyte subsets, cytokines, and the pulmonary inflammation index in coronavirus (COVID-19) infected patients. Br J Haematol 2020;189:428-37.*
6. *Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, et al. Dysregulation of Immune Response in Patients With Coronavirus 2019 (COVID-19) in Wuhan, China. Clin Infect Dis 2020;71:762-8.*
7. *Imam Z, Odish F, Gill I, O'Connor D, Armstrong J, Vanood A, et al. Older age and comorbidity are independent mortality predictors in a large cohort of 1305 COVID-19 patients in Michigan, United States. J Intern Med 2020;288:469-76.*
8. *WHO. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected: interim guidance. 2020.*
9. *Lazzeri C, Bonizzoli M, Batacchi S, Cianchi G, Franci A, Fulceri G,. et al. Cardiac Involvment in COVID-19-Related Acute Respiratory Distress Syndrome. Am J Cardiol 2020;132:147-9.*
10. *Katar M, Beyhan M, Demir O. Could Eosinophil Cationic Protein Be A Useful Biomarker In The Diagnosis Of Covid-19? Sakarya Med J 2021;2:328-336.*
11. *Shah P, Doshi R, Chenna A, Owens R, Cobb A, Ivey H, et al. Prognostic Value of Elevated Cardiac Troponin I in Hospitalized Covid-19 Patients. Am J Cardiol 2020;135:150-3.*
12. *Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. JAMA Cardiol 2020;5:802-10.*
13. *Pareek M, Singh A, Vadlamani L, Eder M, Pacor J, Park J, et al. Relation of Cardiovascular Risk Factors to Mortality and Cardiovascular Events in Hospitalized Patients With Coronavirus Disease 2019 (from the Yale COVID-19 Cardiovascular Registry). Am J Cardiol 2021 Feb 1:S0002-9149(21)00100-4.*
14. *Malik P, Patel U, Patel NH, Somi S, Singh J. Elevated cardiac troponin I as a predictor of outcomes in COVID-19 hospitalizations: a meta-analysis. Infez Med 2020;28:500-6.*
15. *Aghagoli G, Gallo Marin B, Soliman LB, Sellke FW. Cardiac involvement in COVID-19 patients: Risk factors, predictors, and complications: A review. J Card Surg 2020;35:1302-5.*
16. *Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell 2020;181:271-80.*
17. *Zou X, Chen K, Zou J, Han P, Hao J, Han Z. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. Front Med 2020;14:185-92.*
18. *Fung G, Luo H, Qiu Y, Yang D, McManus B. Myocarditis. Circ Res 2016;118:496-514.*
19. *Alhogbani T. Acute myocarditis associated with novel Middle east respiratory syndrome coronavirus. Ann Saudi Med 2016;36:78-80.*
20. *Barman HA, Atici A, Sahin I, Alici G, Aktas Tekin E, Baycan ÖF, et al. Prognostic significance of cardiac injury in COVID-19 patients with and without coronary artery disease. Coron Artery Dis 2020 Jun 19:10.1097/MCA.0000000000000914.*